REMARKS

The present amendment cancels many claims and places the application in condition for allowance or in better form for consideration on appeal. Therefore, in accordance with MPEP §714.12, Applicants respectfully request that the present amendment be entered.

Claims 1-15 and 23-43 are canceled. Applicants reserve the right to pursue any of the canceled subject matter in one or more continuing applications. Claim 19 has been amended merely to correct a technical error in Markush claim format. Claims 16-22 are pending and under examination.

Rejections Under 35 U.S.C. §102

Claims 1-2 and 4-6 are rejected as anticipated by Ceolotto. These claims are canceled without prejudice, thereby rendering the rejection moot.

Rejections Under 35 U.S.C. §103

Claims 16-38 are rejected as being unpatentable over Ceolotto. Claims 23-38 are canceled, thereby obviating their rejection. The rejection is traversed with regard to the presently pending claims. The pending claims are narrowly drawn to a method of evaluating a subject for the extent, stage, or severity of a cardiovascular complication of diabetes. The method includes determining the level of PKC activity in monocytes of the subject, and correlating the level of PKC activity with the extent, stage, or severity of a cardiovascular (CV) complication of diabetes. The Examiner asserts that:

> It is the Examiner's position that Ceolotto discusses the relevance of the study to diabetic complications generally and atherosclerosis specifically. Retinopathy and nephropathy are well known complications of diabetes.

Applicants maintain that Ceolotto's statement that monocytes PKC activity "may be relevant to the study of development of diabetic complications", which the Examiner seems to be referring to in the above-quoted passage, does not suggest a diagnostic correlation, much less a highly specific diagnostic correlation related to the extent, stage, or severity of CV diabetic complications. The Examiner's argument does not address this explicit limitation of the claims at

all and, in fact, seems to ignore this limitation in his argumentation. In particular, the office action does not point out what in Coeletto would make a correlation of monocyte PKC activity with extent, stage, or severity of CV diabetic complications obvious.

Indeed, the claims relate to a completely different patient population than that examined in Ceolotto. The Examiner is reminded that the type 2 diabetic subjects of the Ceolotto study were **free of peripheral vascular disease, free of atherosclerotic cardiovascular disease and "[p]atients with proliferative retinopathy or significant renal impairment [i.e., nephropathy] were also excluded"** from the subject population (see Ceolotto, paragraph bridging pages 1316-1317 and page 1317, first full paragraph of first column). Thus, Ceolotto purposely excluded the particular patient population (those having CV complication of diabetes) recited in the present claims. A skilled artisan would surely not make predictions about a particular patient population based on a study where that specific patient population was excluded. Indeed, the fact that patients having CV complications of diabetes were excluded at all in Ceolotto shows that such patients might be expected to affect the results in an unpredictable manner. In sum, because patients with CV complications were not even part of Ceolottos' study, Ceolotto does not provide the required motivation and reasonable expectation of success to correlate monocyte PKC activity with CV diabetes complications, much less more narrowly with extent, stage, or severity of such complications, as claimed, and even less the specific CV complications recited in the dependent claims.

Enclosed is a Petition for Extension of Time along with the required fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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